fluorescent dye at its 5' terminus, and (iii) is linked to a primary amine group at its 3' terminus, under conditions permitting hybridization between the single stranded nucleic acid which comprises the fluorescent dye and the third oligonucleotide,

wherein hybridization between the single stranded nucleic acid which comprises the fluorescent dye and the immobilized third oligonucleotide identifies the sample as one containing a human hepatitis B virus surface antigen mutant 145.

cont'd.

REMARKS

Claims 69-105 are pending in the subject application. By this Amendment, applicants have canceled claim 86 and have amended claim 85. Accordingly, claims 69-85 and 87-105 will be pending and under examination in the subject application upon entry of this Amendment.

Applicants have annexed hereto a marked-up version of the amended claim as **Exhibit A.**

In view of the arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 85, 87-92, 94 and 95 under 35 U.S.C. §112, first paragraph, as allegedly containing subject

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner alleges that claim 85 as written is not enabled for any "third oligonucleotide", as set forth in step (D)(i), that comprises a mutation present in a human mutant hepatitis B virus, other than the mutation at the amino acid at position 145 of the human hepatitis B virus surface antigen.

In response, applicants respectfully traverse the Examiner's rejection. Specifically, applicants note that claim 85 as amended, provides a method for identifying a human hepatitis B virus antigen mutant 145 wherein the third nucleotide of step (D)(i) comprises a mutation present at the amino acid at position 145 of the human hepatitis B surface antigen. Thus, the Examiner's rejection is obviated.

In view of these remarks, applicants maintain that claims 85, 87-92, 94 and 95 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §103(a)

The Examiner rejected claims 69-105 under 35 U.S.C. §103(a) as being allegedly unpatentable over Stuyver et al (WO 97/40193) in view of Guo et al. (Nucleic Acids Research 22(24):5456-5465, 1994), and McCasky Feazel et al. (U.S. Patent No. 6,100,030).

In considering the arguments set forth by applicants in the

Amendment filed on August 6, 2002 that each and every element must be taught to establish a *prima facie* case of obviousness, the Examiner notes that the rejection was made under 35 U.S.C. §103 not §102. The Examiner further concedes that the identical probes and primers are not taught, but that the importance of detecting mutants is recognized.

In response, applicants respectfully traverse the Examiner's rejection, and again maintain that the Examiner has failed to establish a *prima facie* case of obviousness. Applicants direct the Examiner's attention to M.P.E.P §2143.03, which states that "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Further, according to M.P.E.P. §2143, to establish a *prima facie* case of obviousness, the Examiner must demonstrate three criteria with respect to each claim. First, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

In light of these requirements, applicants maintain that the cited references fail to support a *prima facie* case of obviousness for claims 69-105.

Claims 69-105 provide oligonucleotides linked to fluorescent

dyes and primary amine groups, compositions comprising same and methods for identifying the human hepatitis B virus surface antigen mutant 145 and the wildtype human hepatitis B surface antigen using the claimed oligonucleotides. These claims are based, at least in part, on applicants' novel oligonucleotides that may be used to amplify the human hepatitis B virus surface antigen mutant 145, thereby enabling its detection in serum samples.

The cited references, in combination, fail to teach each and every element of the instant claims. In particular, the references fail to teach the oligonucleotide sequences (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7) as set forth in the claims. As the Examiner concedes, Stuyver et al. only teaches a method of detecting mutant human hepatitis B virus but does not disclose specific fluorescent labels as set forth in claims 71, 77, 83, 84, 89, 93, 94, 99, 103 and 104, the addition of a C-7 primary amine as set forth in claims 72, 78, 90, 93, 100 and 103, or the specific oligonucleotide sequences as set forth in claims 69, 70, 75, 76, 81, 82, 84, 85, 87, 88, 93, 96, 97, 98 and 103. Moreover, Guo et al. and McCasky Feazel et al. also fail to teach these recited elements. Although these references teach certain techniques pertaining to the instant methods, none teaches the oligonucleotide sequences recited in the instant claims.

For the reasons stated above, the combined cited references fail to teach the elements of the claimed oligonucleotides, compositions and methods. Moreover, absent such teaching, there could not have been a motive to combine or a reasonable

expectation of success.

In view of the above remarks, applicants maintain that the Examiner has failed to set forth a *prima facie* case of obviousness, and that accordingly, claims 69-105 satisfy the requirements of 35 U.S.C. §103(a).

Conclusion

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and earnestly solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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Marked-Up Version of Claim 85:

85. (Amended) A method for identifying a human hepatitis B virus surface antigen mutant 145 in a sample which comprises:

(A) obtaining a viral nucleic acid from the sample;

(B) amplifying the viral nucleic acid in a polymerase chain reaction using two primers, wherein

(1) one primer is a first oligonucleotide which (i) has the sequence AGGATCAACAACAACCAGTA (SEQ ID NO:6), and (ii) is linked at its 5' terminus to a biotin group; and

(2) the other primer is a second oligonucleotide which [(1)] (i) has the sequence ATCGTCCTGGGCTTTCGCAA (SEQ ID NO:7), and [(2)] (ii) is linked at its 5' terminus to a fluorescent dye;

(C) obtaining, from the amplified nucleic acid, single stranded nucleic acid which comprises the fluorescent dye; and

(D) contacting the single stranded nucleic acid which comprises the fluorescent dye to an immobilized third oligonucleotide, which oligonucleotide comprises a sequence which (i) corresponds to a portion of a human hepatitis B virus surface antigen nucleic acid, which portion comprises a mutation present at the amino acid at position 145 of [in a mutant] human hepatitis B virus surface antigen, (ii) is linked to a fluorescent dye at its 5' terminus, and (iii) is linked to a primary amine group at its 3' terminus, under

conditions permitting hybridization between the single stranded nucleic acid which comprises the fluorescent dye and the third oligonucleotide,

wherein hybridization between the single stranded nucleic acid which comprises the fluorescent dye and the immobilized third oligonucleotide identifies the sample as one containing a human hepatitis B virus surface antigen mutant 145.